08/793653
PCT/US96/20718

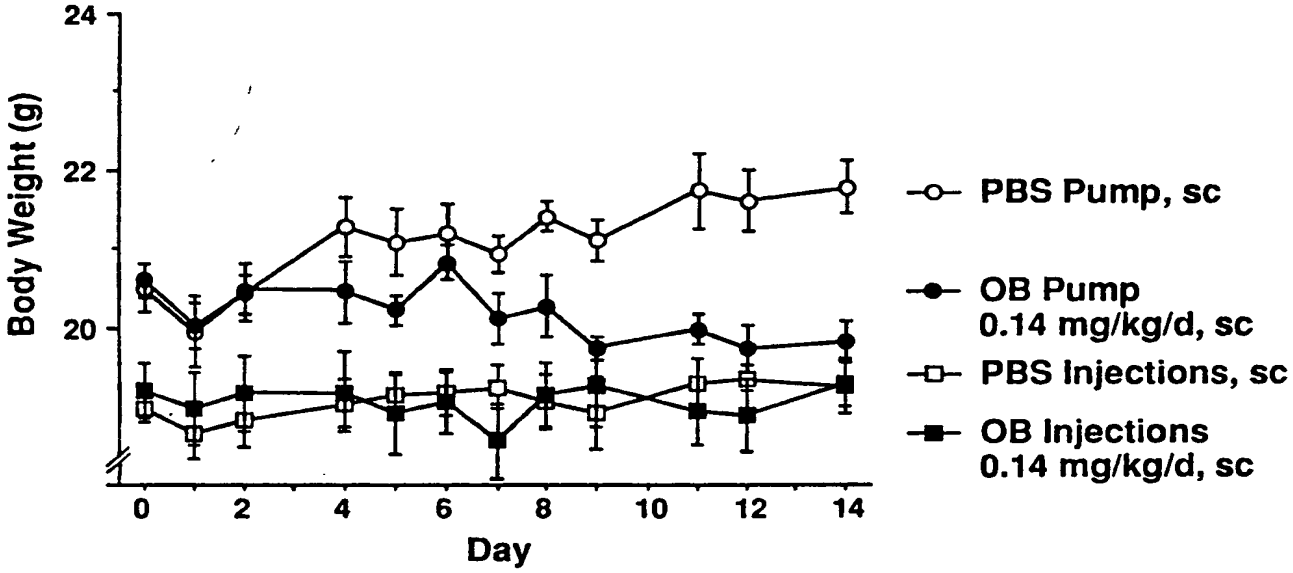

FIG. 1A

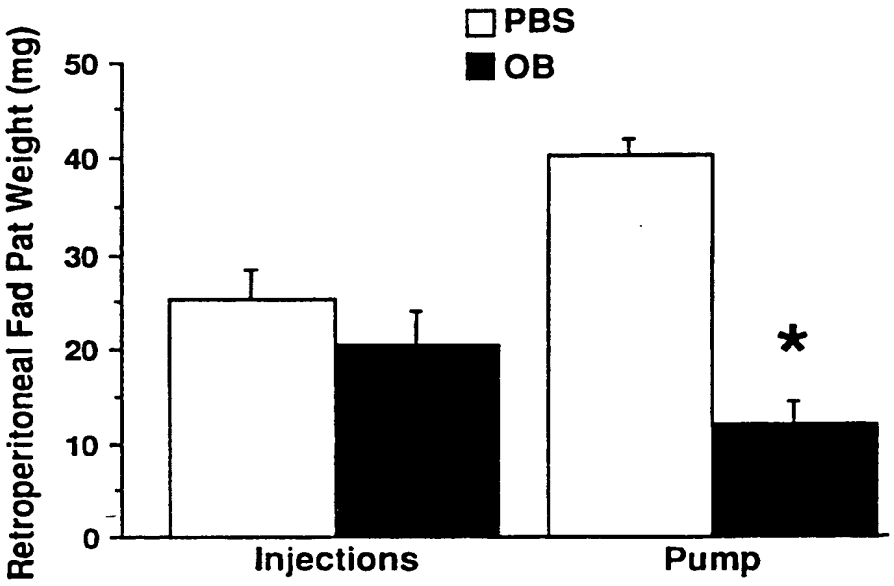

FIG. 1B

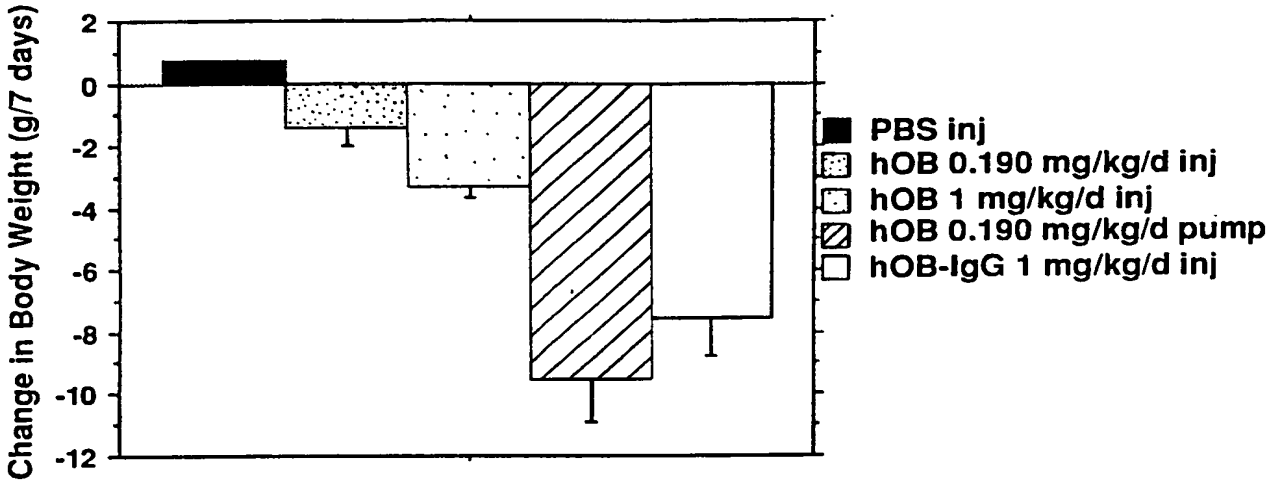

FIG. 2A

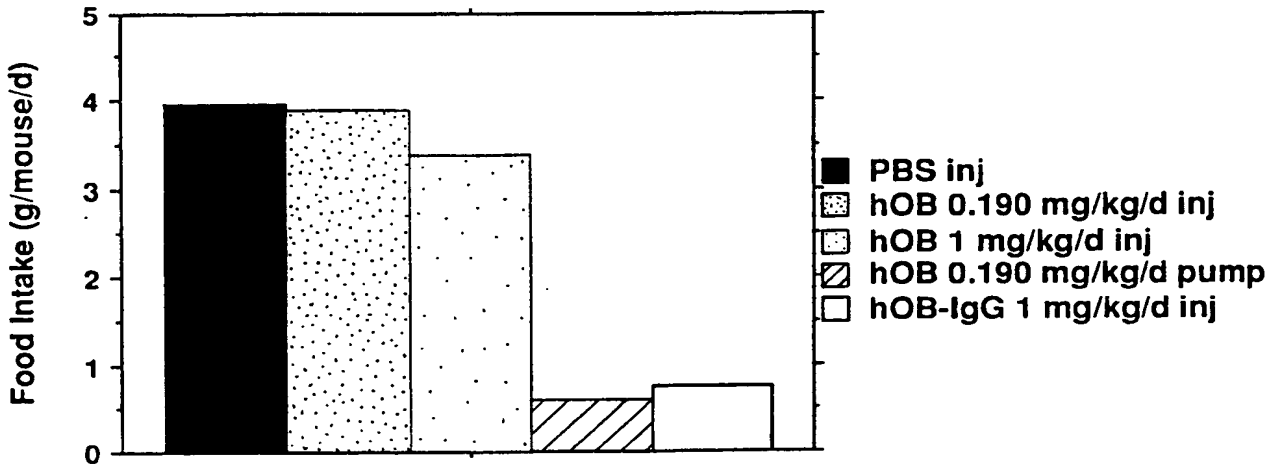

FIG. 2B

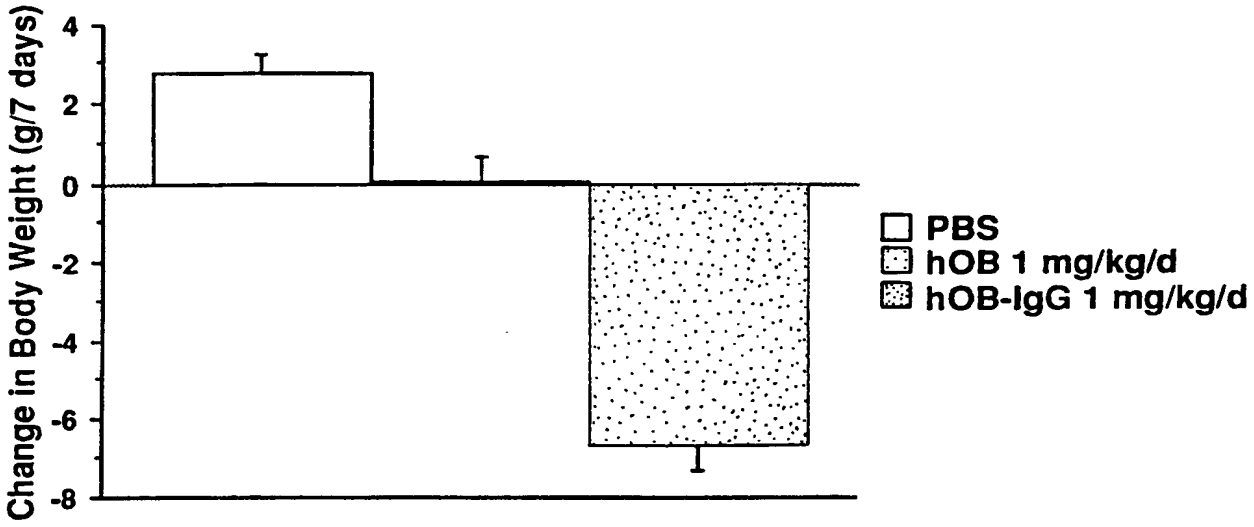

FIG. 3A

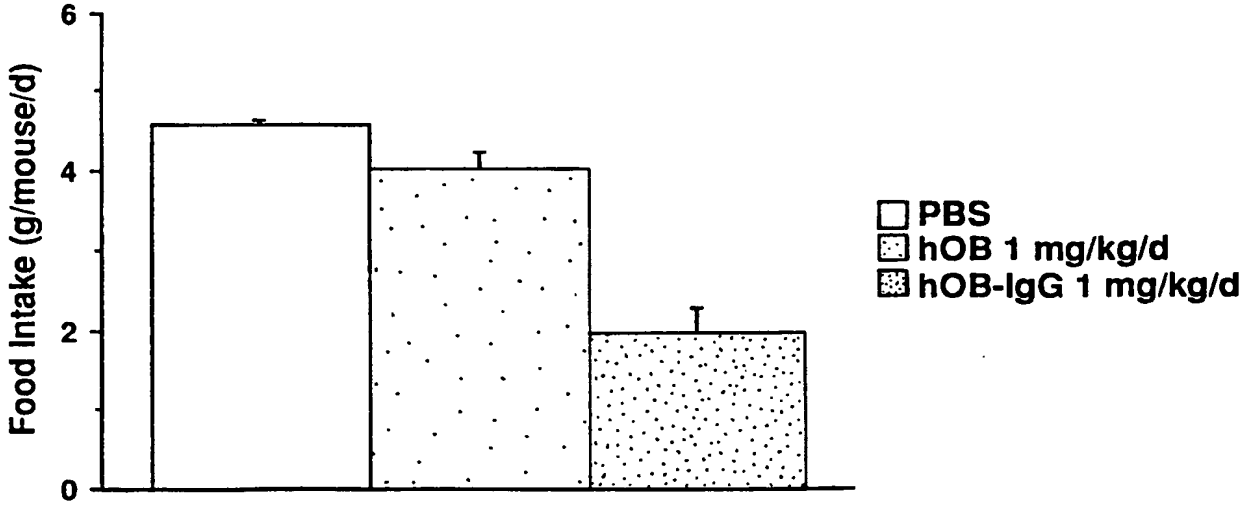

FIG. 3B

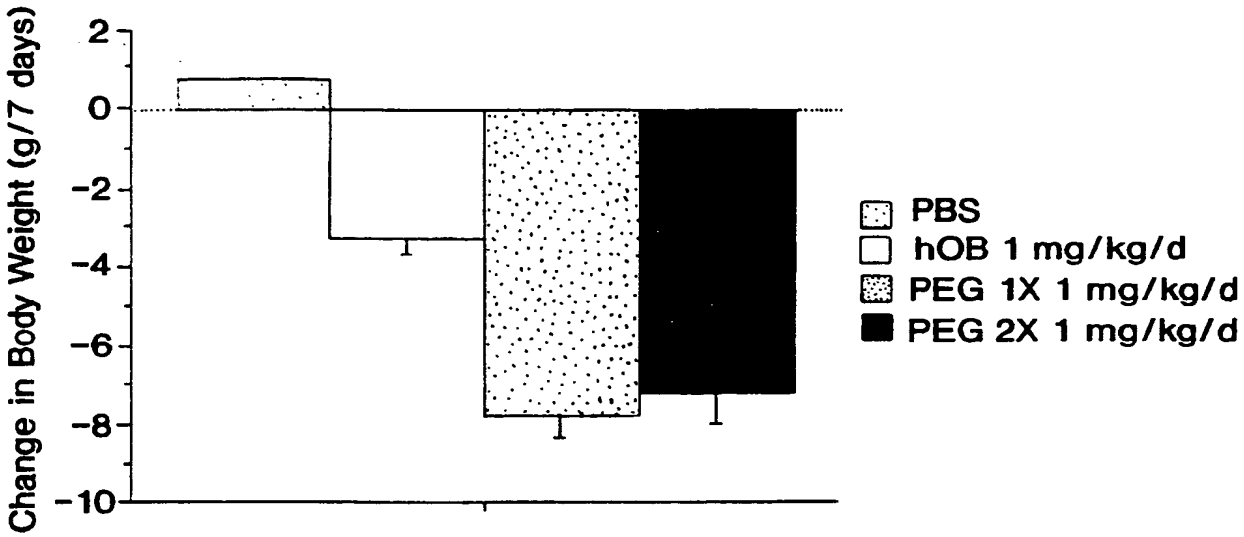

FIG. 4A

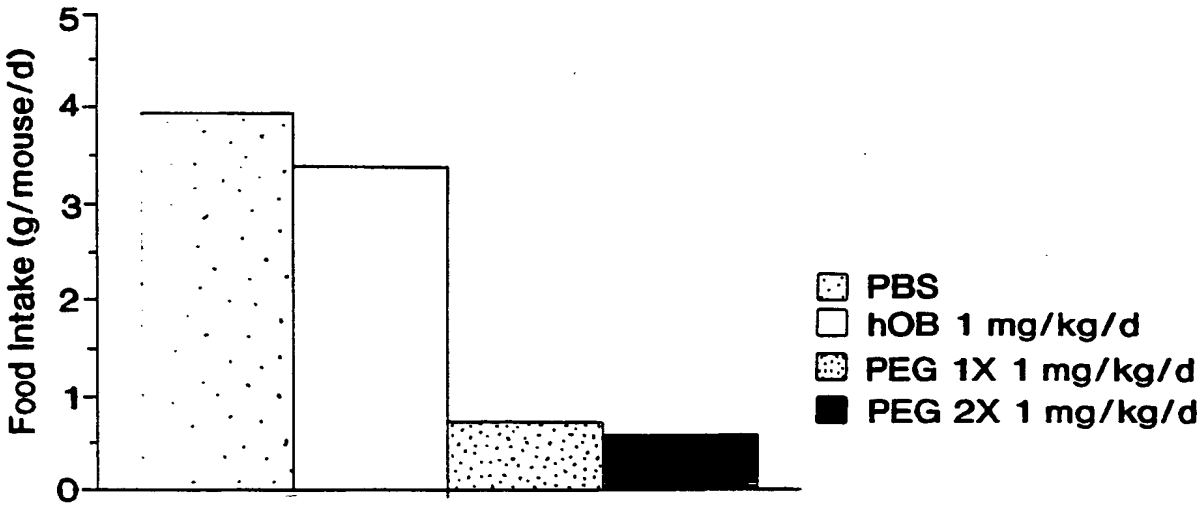

FIG. 4B

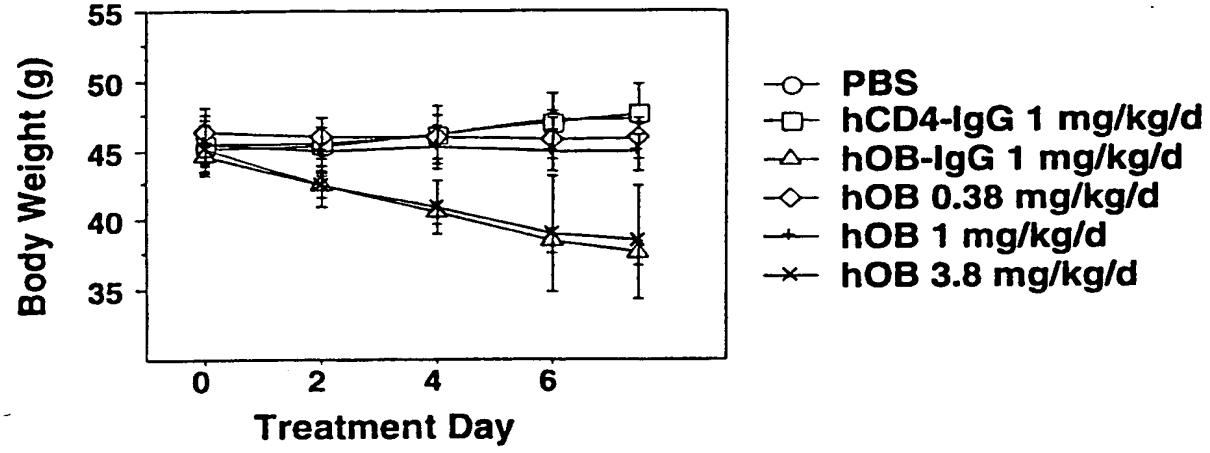

FIG. 5A

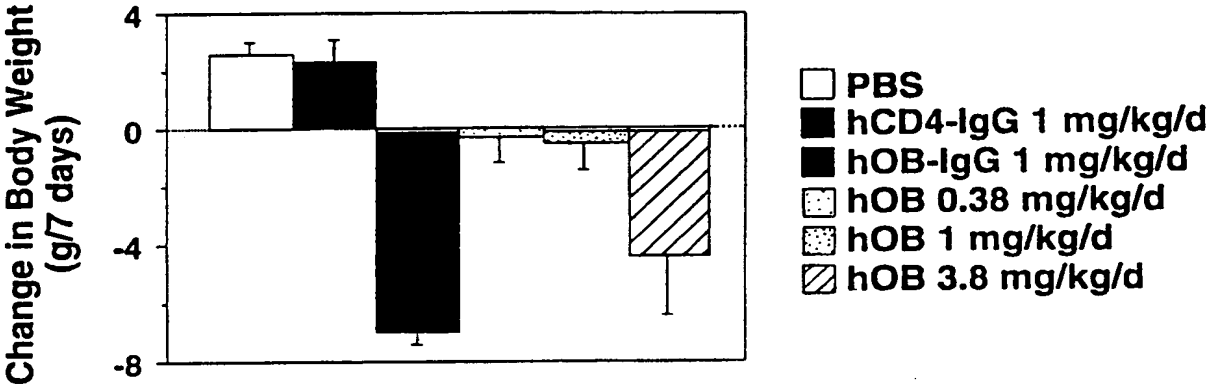

FIG. 5B

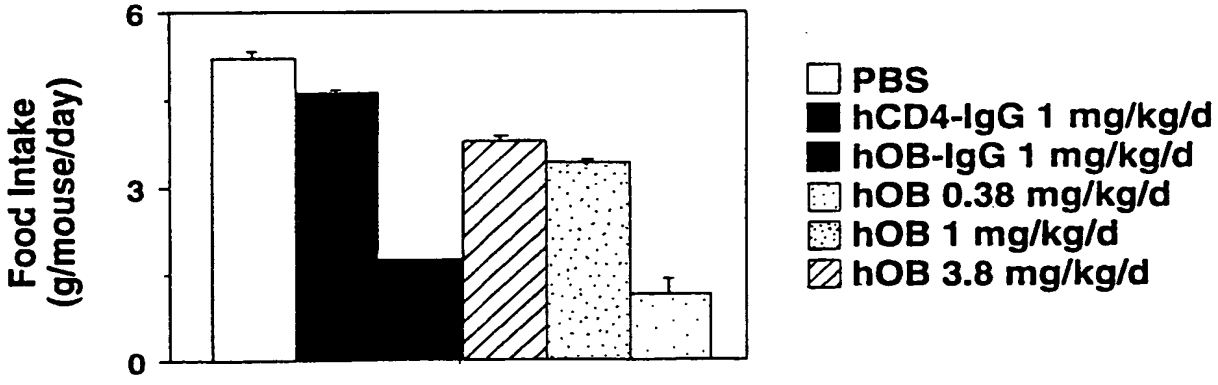

FIG. 5C

APPROVED BY DRAFTSMAN | O.G. FIG. | CLASS | SUBCLASS
WO 97/24440

08/793653
PCT/US96/20718


```
                                            ss.pRK5tkneo.hOBIgG
>
> sites: std
> length: 7127 (circular)
>
>human OB ClaI/BstEII cloning
>CMV enhancer/promoter

       aluI
      sstI
      sacI
      hgiJII
      hgiAI/aspHI
      ecl136II
      bsp1286
      bsiHKAI
      bmyI                        rmaI    tru9I                                                  thaI
      banII                       maeI    mseI                                                   fnuDII/mvnI
     taqI                        speI    aseI/asnI/vspI                      bslI                bstUI
                                                                                                 bsh1236I
                                                                                                aciI maeIII
  1 TTCGAGCTCG CCCGACATTG ATTATTGACT AGTTATTAAT AGTAATCAAT TACGGGGTCA TTAGTTCATA GCCCATATAT GGAGTTCCGC GTTACATAAC
    AAGCTCGAGC GGGCTGTAAC TAATAACTGA TCAATAATTA TCATTAGTTA ATGCCCCAGT AATCAAGTAT CGGGTATATA CCTCAAGGCG CAATGTATTG

                      scrFI
                      mvaI
                      ecoRII
                      dsaV
                   aciI
                 bglI bstNI                                  maeII
                sau96I                                     hinlI/acyI
                haeIII/palI     aciI                       ahaII/bsaHI
                asuI  apyI[dcm+]            aciI           aatII         maeII           maeIII
101 TTACGGTAAA TGGCCCGCCT GGCTGACCGC CCAACGACCC CCGCCCATTG ACGTCAATAA TGACGTATGT TCCCATAGTA ACGCCAATAG GGACTTTCCA
    AATGCCATTT ACCGGGCGGA CCGACTGGCG GGTTGCTGGG GGCGGGTAAC TGCAGTTATT ACTGCATACA AGGGTATCAT TGCGGTTATC CCTGAAAGGT

       maeII                                                                                      maeII
      hinlI/acyI                                                                                 hinlI/acyI
      ahaII/bsaHI                                     rsaI                 rsaI                  ahaII/bsaHI
      aatII                          bglI             csp6I           ndeI   csp6I               aatII
201 TTGACGTCAA TGGGTGGAGT ATTTACGGTA AACTGCCCAC TTGGCAGTAC ATCAAGTGTA TCATATGCCA AGTACGCCCC CTATTGACGT CAATGACGGT
    AACTGCAGTT ACCCACCTCA TAAATGCCAT TTGACGGGTG AACCGTCATG TAGTTCACAT AGTATACGGT TCATGCGGGG GATAACTGCA GTTACTGCCA
```

FIG. 6A

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```
              scrFI
              mvaI
              ecoRII
          aciI                                                                              nlaIII
        bglI  dsaV                                                                   styI
       sau96I bstNI          rsaI                                     maeII                ncoI
       haeIII/palI           csp6I                            rsaI   snaBI                 dsaI hphI aciI
       asuI   apyI(dcm+) bsrI  nlaIII                         csp6I  bsaAI                 bsaJI  sfaNI
301 AAATGGCCCG CCTGGCATTA TGCCCAGTAC ATGACCTTAT GGGACTTTCC TACTTGGCAG TACATCTACG TATTAGTCAT CGCTATTACC ATGGTGATGC
    TTTACCGGGC GGACCGTAAT ACGGGTCATG TACTGGAATA CCCTGAAAGG ATGAACCGTC ATGTAGATGC ATAATCAGTA GCGATAATGG TACCACTACG

                                                                            maeII
                                                                           hinII/acyI            nlaIV
              rsaI                       pleI                              ahaII/bsaHI           hgiCI
              csp6I                aciI  hinfI              bsmAI          aatII                 banI
401 CGTTTTGGCA GTACATCAAT GGGCGTGGAT AGCGGTTTGA CTCACGGGGA TTTCCAAGTC TCCACCCCAT TGACGTCAAT GGGAGTTTGT TTTGGCACCA
    CCAAAACCGT CATGTAGTTA CCCGCACCTA TCGCCAAACT GAGTGCCCCT AAAGGTTCAG AGGTGGGGTA ACTGCAGTTA CCCTCAAACA AAACCGTGGT

                                                                                                aluI
                                                                                                sstI
                                                                                                sacI
                                                                                                hgiJII
                                                                                                hgiAI/aspHI
                                                                                                ecl136II
                                                                                                bsp1286
                                                                                                bsiHKAI
                                                                      rsaI                      bmyI
                             maeIII   aciI       hgaI       aciI      csp6I    mnlI             banII
501 AAATCAACGG GACTTTCCAA AATGTCGTAA CAACTCCGCC CCATTGACGC AAATGGGCGG TAGGCGTGTA CGGTGGGAGG TCTATATAAG CAGAGCTCGT
    TTTAGTTGCC CTGAAAGGTT TTACAGCATT GTTGAGGCGG GGTAACTGCG TTTACCCGCC ATCCGCACAT GCCACCCTCC AGATATATTC GTCTCGAGCA
```

FIG. 6B

08/793653
PCT/US96/20718


```
                                                                                                haeIII/palI
                                                                                               mcrI
                                                                                               eagI/xmaIII/eclXI
                                                                                               eaeI
                                                                                               cfrI
                                                                                              fnu4HI
                                                                                              aciI
                                                                                             thaI
                                                                                             fnuDII/mvnI
                             esp3I                                   sau96I           sacII/sstII
                        scrFI                                              avaII            nspBII
                        mvaI bsmAI
                        ecoRII                                       asuI             kspI  scrFI
                        dsaV                                        nlaIV             dsaI  nciI
                        bstNI  hinlI/acyI                               scrFI          bglI bslI  mspI
                        apyI(dcm+)                                      nciI     sau3AI mnlI bstUI
                   sau3AI gsuI/bpmI                                     mspI     mboI/ndeII(dam-] hpaII
                   mboI/ndeII(dam-]                             mboII   hpaII    dpnI(dam+]  bsaJI dsaV
                   dpnI(dam+]  hgaI  fokI                       bpuAI   dsaV     dpnII(dam-] bsh1236I
                   dpnII(dam-] ahaII/bsaHI             mnlI     bbsI    cauII    alwI(dam-]  aciI cauII
601 TTAGTGAACC GTCAGATCGC CTGGAGACGC CATCCACGCT GTTTTGACCT CCATAGAAGA CACCGGGACC GATCCAGCCT CCGCGGCCGG GAACGGTGCA
    AATCACTTGG CAGTCTAGCG GACCTCTGCG GTAGGTGCGA CAAAACTGGA GGTATCTTCT GTGGCCCTGG CTAGGTCGGA GGCGCCGGCC CTTGCCACGT
                ^Begin RNA

               tfiI                                                                             fnu4HI
           aciI                                                                                 aciI
          thaI hinfI                                          bstXI                            thaI
          fnuDII/mvnI                         aciI                sau96I    styI               fnuDII/mvnI tru9I
          bstUI                      maeII rsaI            pleI scfI haeIII/palI               bstUI       mseI
          bsh1236I               maeIII    csp6I   scfI hinfI     asuI      bsaJI              bsh1236I   aseI/asnI/vspI
701 TTGGAACGCG GATTCCCCGT GCCAAGAGTG ACGTAAGTAC CGCCTATAGA GTCTATAGCC CCACCCCCTT GGCTTCGTTA GAACGCGGCT ACAATTAATA
    AACCTTGCGC CTAAGGGGCA CGGTTCTCAC TGCATTCATG GCGGATATCT CAGATATCCG GGTGGGGGAA CCGAAGCAAT CTTGCGCCGA TGTTAATTAT
                                                                                      ^sp6 promoter
```

FIG. 6C

```
                                                                                                               sau96I
                                                                                                               avaII
                                                                                                               asuI
                                                                                                            scrFI
                                                                                                            mvaI
                                                                                                            ecoRII
                                                                                                            dsaV
                                                                                                            bstNI
                                                  maeIII                                                    apyI[dcm+]
                                                 hphI    scfI          fokI                             bslI bsaJI
801 CATAACCTTA TGTATCATAC ACATACGATT TAGGTGACAC TATAGAATAA CATCCACTTT GCCTTTCTCT CCACAGGTGT CCACTCCCAG GTCCAACTGC
    GTATTGGAAT ACATAGTATG TGTATGCTAA ATCCACTGTG ATATCTTATT GTAGGTGAAA CGGAAAGAGA GGTGTCCACA GGTGAGGGTC CAGGTTGACG
                                                                 ^sp6 RNA start

                                ppu10I                  tfiI              sau96I
     mnlI           taqI nsiI/avaIII                    hinfI             haeIII/palI                   bsp1286
     bsaJI         claI/bsp106     nlaIV          aciI                    asuI                     aluI bmyI fokI
901 ACCTCGGTTC TATCGATATG CATTGGGGAA CCCTGTGCGG ATTCTTGTGG CTTTGGCCCT ATCTTTTCTA TGTCCAAGCT GTGCCCATCC AAAAAGTCCA
    TGGAGCCAAG ATAGCTATAC GTAACCCCTT GGGACACGCC TAAGAACACC GAAACCGGGA TAGAAAAGAT ACAGGTTCGA CACGGGTAGG TTTTTCAGGT
  1                       Met HisTrpGlyT hrLeuCysGl yPheLeuTrp LeuTrpProT yrLeuPheTy rValGlnAla ValProIleG lnLysValGln
     ^cloning linker  ^human OB start

                                                        sau3AI
                                                        mboI/ndeII[dam-]
                                                        dpnI[dam+]
                                                    scrFI
                                                    mvaI                                                        mspI
                                                    ecoRII                                                 hpaII
                                                    dsaV                                                  cfr10I
                                                    bstNI                                                      bsaWI
                                                    apyI[dcm+]                                                 ageI
                                                 hphI   dpnII[dam-]                        mnlI              hphI
                                  mnlI        munI  maeIII alwI[dam-]                  bsmAI                maeIII
1001 AGATGACACC AAAACCCTCA TCAAGACAAT TGTCACCAGG ATCAATGACA TTTCACACAC GCAGTCAGTC TCCTCCAAAC AGAAAGTCAC CGGTTTGGAC
     TCTACTGTGG TTTTGGGAGT AGTTCTGTTA ACAGTGGTCC TAGTTACTGT AAAGTGTGTG CGTCAGTCAG AGGAGGTTTG TCTTTCAGTG GCCAAACCTG
  29  AspAspThr LysThrLeuI leLysThrIl eValThrArg IleAsnAspI leSerHisTh rGlnSerVal SerSerLysG lnLysValTh rGlyLeuAsp
```

FIG. 6D

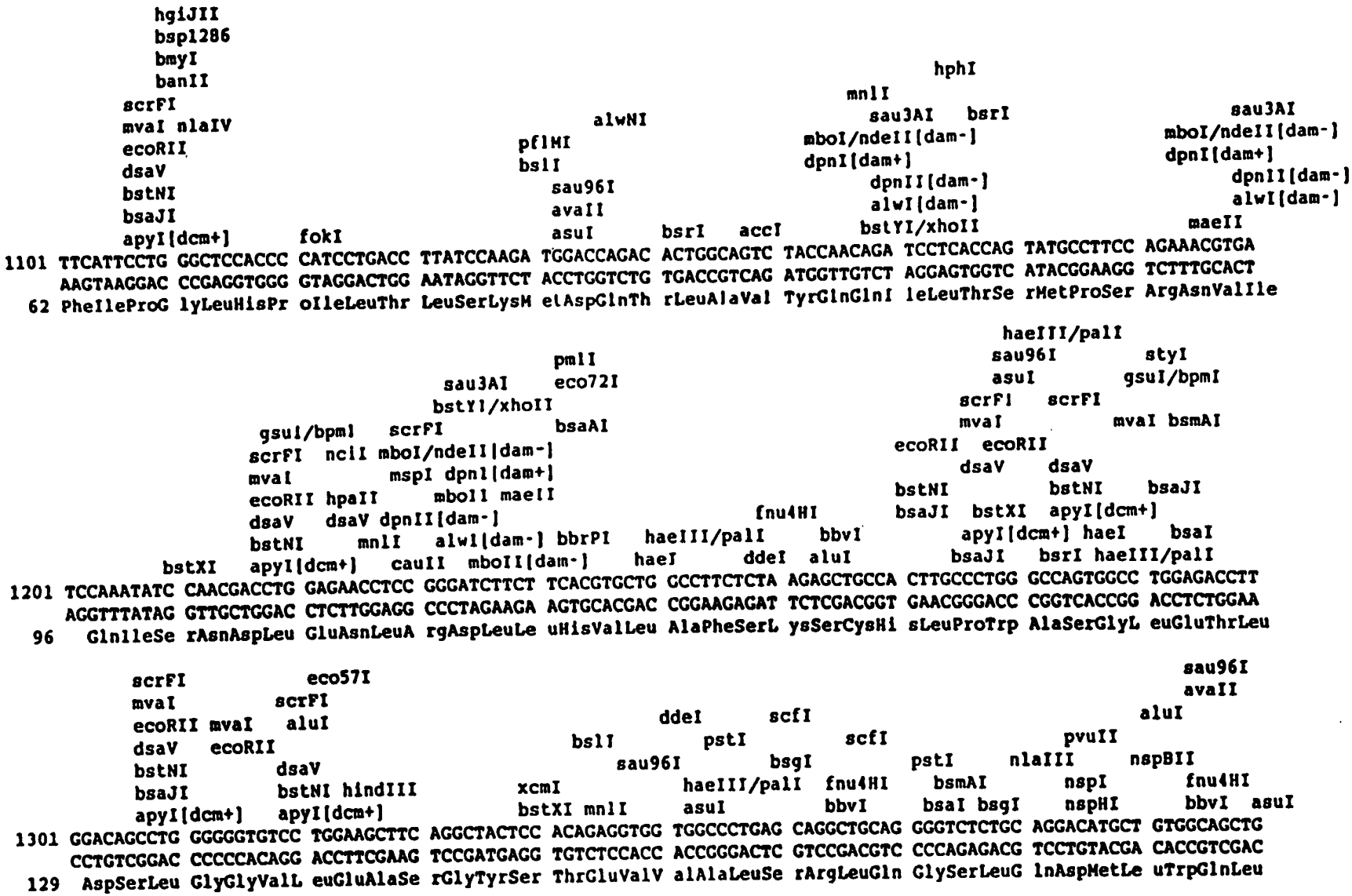

FIG. 6E

08/793653
PCT/US96/20718

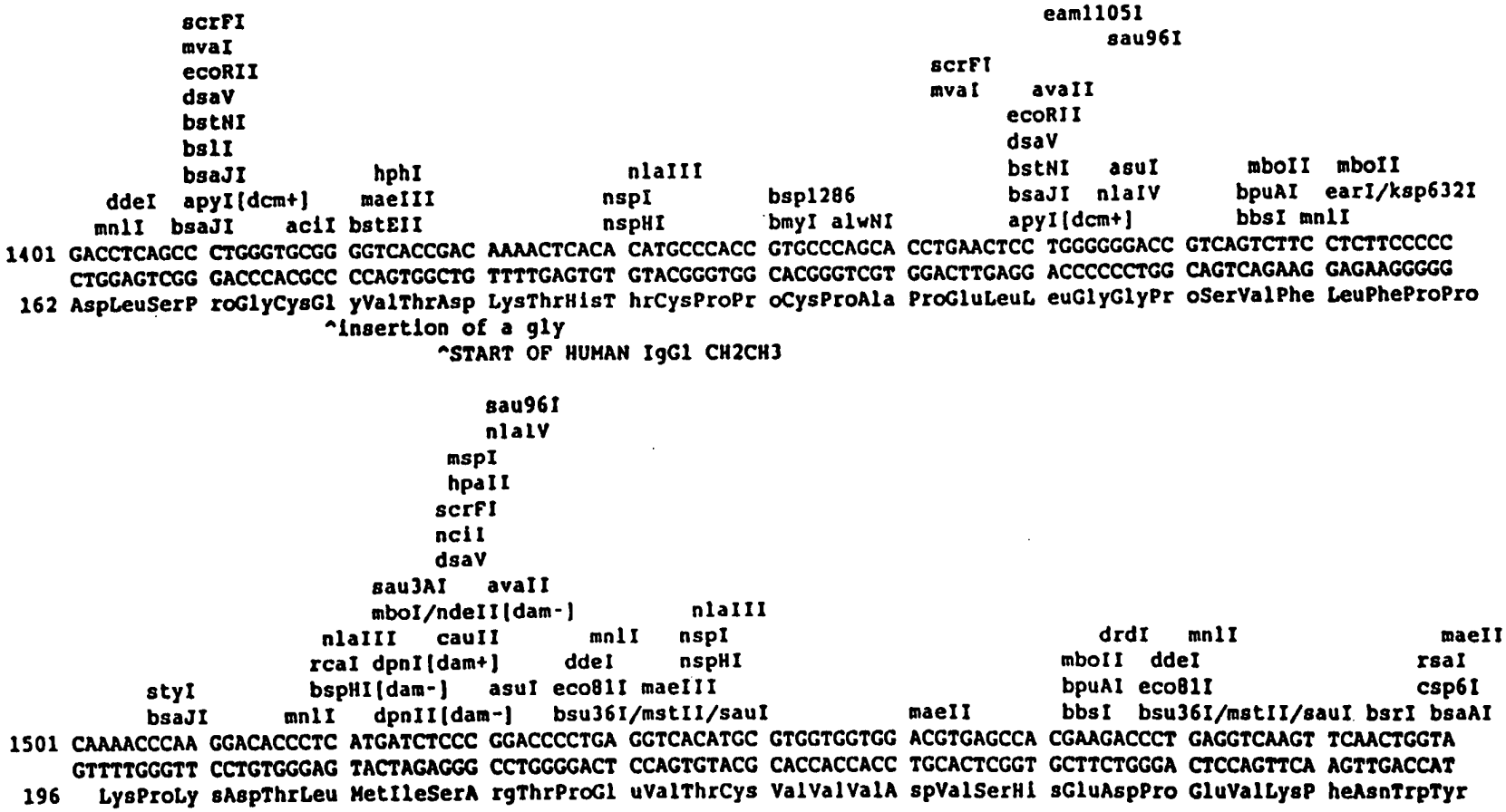

FIG. 6F

```
                                               aciI
                                              thaI
                                              fnuDII/mvnI
                                              bstUI
                                              bsh1236I
                                             sacII/sstII
                                             nspBII                                                            scrFI
                                             kspI                                                              mvaI
                                             dsaI                          rsaI                                ecoRII
                                             bsaJI                         csp6I                               dsaV
                                             aciI             rsaI       maeII                   hphI       ecoNI bstNI
                   mnlI                     fnu4HI  mnlI      csp6I     bsaAI             hgaI mnlI      bslI  apyI[dcm+]
1601 CGTGGACGGC GTGGAGGTGC ATAATGCCAA GACAAAGCCG CGGGACGAGC AGTACAACAG CACGTACCGT GTGGTCAGCG TCCTCACCGT CCTGCACCAG
     GCACCTGCCG CACCTCCACG TATTACGGTT CTGTTTCGGC GCCCTCCTCG TCATGTTGTC GTGCATGGCA CACCAGTCGC AGGAGTGGCA GGACGTGGTC
 229  ValAspGly ValGluValH isAsnAlaLy sThrLysPro ArgGluGluG lnTyrAsnSe rThrTyrArg ValValSerV alLeuThrVa lLeuHisGln

                           rsaI          bsmAI                                                         fnu4HI
      bsrI                 csp6I        bsaI            mnlI             taqI                          bbvI  avaI
1701 GACTGGCTGA ATGGCAAGGA GTACAAGTGC AAGGTCTCCA ACAAAGCCCT CCCAGCCCCC ATCGAGAAAA CCATCTCCAA AGCCAAAGGG CAGCCCCGAG
     CTGACCGACT TACCGTTCCT CATGTTCACG TTCCAGAGGT TGTTTCGGGA GGGTCGGGGG TAGCTCTTTT GGTAGAGGTT TCGGTTTCCC GTCGGGGCTC
 262 AspTrpLeuA snGlyLysGl uTyrLysCys LysValSerA snLysAlaLe uProAlaPro IleGluLysT hrIleSerLy sAlaLysGly GlnProArgGlu

                                   scrFI
                                   nciI
                                   mspI
                                   hpaII
                                   dsaV
                                   cauII
                                  xmaI/pspAI
                                  smaI
                                  scrFI                    scrFI         scrFI
                                  nciI                     mvaI                mvaI
                                  dsaV                     ecoRII        ecoRII
                                  cauII                    dsaV          dsaV
                rsaI           fokI                        bstNI               bstNI                              dsaI
                csp6I        bslI bsaJI mboII              apyI[dcm+]          apyI[dcm+]                         bslI
              bsp1407I      bslI  avaI  earI/ksp632I      sexAI           bspMI                                   bsaJI
1801 AACCACAGGT GTACACCCTG CCCCCATCCC GGGAAGAGAT GACCAAGAAC CAGGTCAGCC TGACCTGCCT GGTCAAAGGC TTCTATCCCA GCGACATCGC
     TTGGTGTCCA CATGTGGGAC GGGGGTAGGG CCCTTCTCTA CTGGTTCTTG GTCCAGTCGG ACTGGACGGA CCAGTTTCCG AAGATAGGGT CGCTGTAGCG
 296   ProGlnVa lTyrThrLeu ProProSerA rgGluGluMe tThrLysAsn GlnValSerL euThrCysLe uValLysGly PheTyrProS erAspIleAla
```

FIG. 6G

```
                                mspI                                                                           dsaI
                                hpaII                                   pleI                  mnlI          hphI
                            fnu4HI                                                                     
                            bbvI                         mnlI          hinfI     nlaIV  mboII    scfI   aluI  bsaJI
1901 CGTGGAGTGG GAGAGCAATG GGCAGCCGGA GAACAACTAC AAGACCACGC CTCCCGTGCT GGACTCCGAC GGCTCCTTCT TCCTCTACAG CAAGCTCACC
     GCACCTCACC CTCTCGTTAC CCGTCGGCCT CTTGTTGATG TTCTGGTGCG GAGGGCACGA CCTGAGGCTG CCGAGGAAGA AGGAGATGTC GTTCGAGTGG
329   ValGluTrp GluSerAsnG lyGlnProGl uAsnAsnTyr LysThrThrP roProValLe uAspSerAsp GlySerPheP heLeuTyrSe rLysLeuThr

                                                                                                                 scrFI
                                                                                                                 ncil
                                       mboII                                                                     mspI
                                      bpuAI                 nlaIII                                               hpaII
                                   maeII                 ppu10I                                 sapI             dsaV
                       fnu4HI    xmnI bbsI               nsiI/avaIII                            mboII mnlI    bsmAI
                bspHI  bbvI      asp700      nlaIII     sfaNI   mnlI                            earI/ksp632I bslI cauII
2001 GTGGACAAGA GCAGGTGGCA GCAGGGGAAC GTCTTCTCAT GCTCCGTGAT GCATGAGGCT CTGCACAACC ACTACACGCA GAAGAGCCTC TCCCTGTCTC
     CACCTGTTCT CGTCCACCGT CGTCCCCTTG CAGAAGAGTA CGAGGCACTA CGTACTCCGA GACGTGTTGG TGATGTGCGT CTTCTCGGAG AGGGACAGAG
362  ValAspLysS erArgTrpGl nGlnGlyAsn ValPheSerC ysSerValMe tHisGluAla LeuHisAsnH isTyrThrGl nLysSerLeu SerLeuSerPro

                                                                                          sau96I
                                                                                       nlaIII
                                   taqI                                            fnu4HI    haeIII/palI
                                  salI                        taqI                 bglI styI
                                pleI     scfI              pleI     scfI          sfiI  ncoI
                             rmaI hincII/hindII         rmaI  salI  pstI         eaeI  dsaI
                        sau96I  hinfI    pstI          xbaI  hincII/hindII       cfrI  bsaJI                 aluI
                        haeIII/palI      bsgI     aluI maeI  accI   bsgI     aluI haeIII/palI              fnu4HI
                        asuI maeI accI bspHI    hindIII    hinfI  bspHI     hindIII   aciI   asuI          bbvI
2101 CGGGTAAATG AGTGCGACGG CCCTAGAGTC GACCTGCAGA AGCTTCTAGA GTCGACCTGC AGAAGCTTGG CCGCCATGGC CCAACTTGTT TATTGCAGCT
     GCCCATTTAC TCACGCTGCC GGGATCTCAG CTGGACGTCT TCGAAGATCT CAGCTGGACG TCTTCGAACC GGCGGTACCG GGTTGAACAA ATAACGTCGA
396   GlyLys
                                                                                                ^sv40 early poly A

                                                                               rmaI
            maeIII                 sfaNI   apoI                           bsmI maeI
2201 TATAATGGTT ACAAATAAAG CAATAGCATC ACAAATTTCA CAAATAAAGC ATTTTTTTCA CTGCATTCTA GTTGTGGTTT GTCCAAACTC ATCAATGTAT
     ATATTACCAA TGTTTATTTC GTTATCGTAG TGTTTAAACT GTTTATTTCG TAAAAAAAGT GACGTAAGAT CAACACCAAA CAGGTTTGAG TAGTTACATA
```

FIG. 6H

```
                   sau3AI
                   mboI/ndeII[dam-]
                   dpnI[dam+]
                   dpnII[dam-]
                  pvuI/bspCI
                  mcrI
                 taqI[dam-]  tru9I                haeIII/palI                                         rsaI
                claI/bsp106[dam-]                haeI                                                 csp6I
               sau3AI        mseI       fnu4HI styI                                                  nlaIV
               mboI/ndeII[dam-]         bbvI   ncoI                                                  kpnI
               dpnI[dam+] xmnI        hinPI    dsaI                                                  hgiCI
               dpnII[dam-]  aseI/asnI/vspI     bsaJI                                                 banI
                                                                                                     asp718     mnlI
        nlaIII  alwI[dam-]  asp700    hhaI/cfoI nlaIII          mnlI       mnlI                      acc65I  ddeI  aciI
2301 CTTATCATGT CTGGATCGAT CGGGAATTAA TTCGGCGCAG CACCATGGCC TGAAATAACC TCTGAAAGAG GAACTTGGTT AGGTACCTTC TGAGGCGGAA
     GAATAGTACA GACCTAGCTA GCCCTTAATT AAGCCGCGTC GTGGTACCGG ACTTTATTGG AGACTTTCTC CTTGAACCAA TCCATGGAAG ACTCCGCCTT
                          ^sv40 origin

                                                 nlaIV
                                               scrFI                         sfaNI                  scrFI
                                               mvaI                             ppu10I                   mvaI
                                               ecoRII                      nsiI/avaIII              ecoRII
                                               dsaV                       nlaIII                    dsaV
        aluI                                   bstNI                         sphI                        bstNI
       pvuII                                   apyI[dcm+]                    nspI                        apyI[dcm+]
       nspBII                                 bsaJI                          nspHI                      sexAI
2401 AGAACCAGCT GTGGAATGTG TGTCAGTTAG GGTGTGGAAA GTCCCCAGGC TCCCCAGCAG GCAGAAGTAT GCAAAGCATG CATCTCAATT AGTCAGCAAC
     TCTTGGTCGA CACCTTACAC ACAGTCAATC CCACACCTTT CAGGGGTCCG AGGGGTCGTC CGTCTTCATA CGTTTCGTAC GTAGAGTTAA TCAGTCGTTG

                     nlaIV
                   scrFI
                   mvaI                              ppu10I
                   ecoRII                         nsiI/avaIII
                   dsaV                          nlaIII
                   bstNI                             sphI
                   apyI[dcm+]                        nspI sfaNI
                  bsaJI                              nspHI                         aciI       aciI fokI
2501 CAGGTGTGGA AAGTCCCCAG GCTCCCCAGC AGGCAGAAGT ATGCAAAGCA TGCATCTCAA TTAGTCAGCA ACCATAGTCC CGCCCCTAAC TCCGCCCATC
     GTCCACACCT TTCAGGGGTC CGAGGGGTCG TCCGTCTTCA TACGTTTCGT ACGTAGAGTT AATCAGTCGT TGGTATCAGG GCGGGGATTG AGGCGGGTAG
```

FIG. 6I

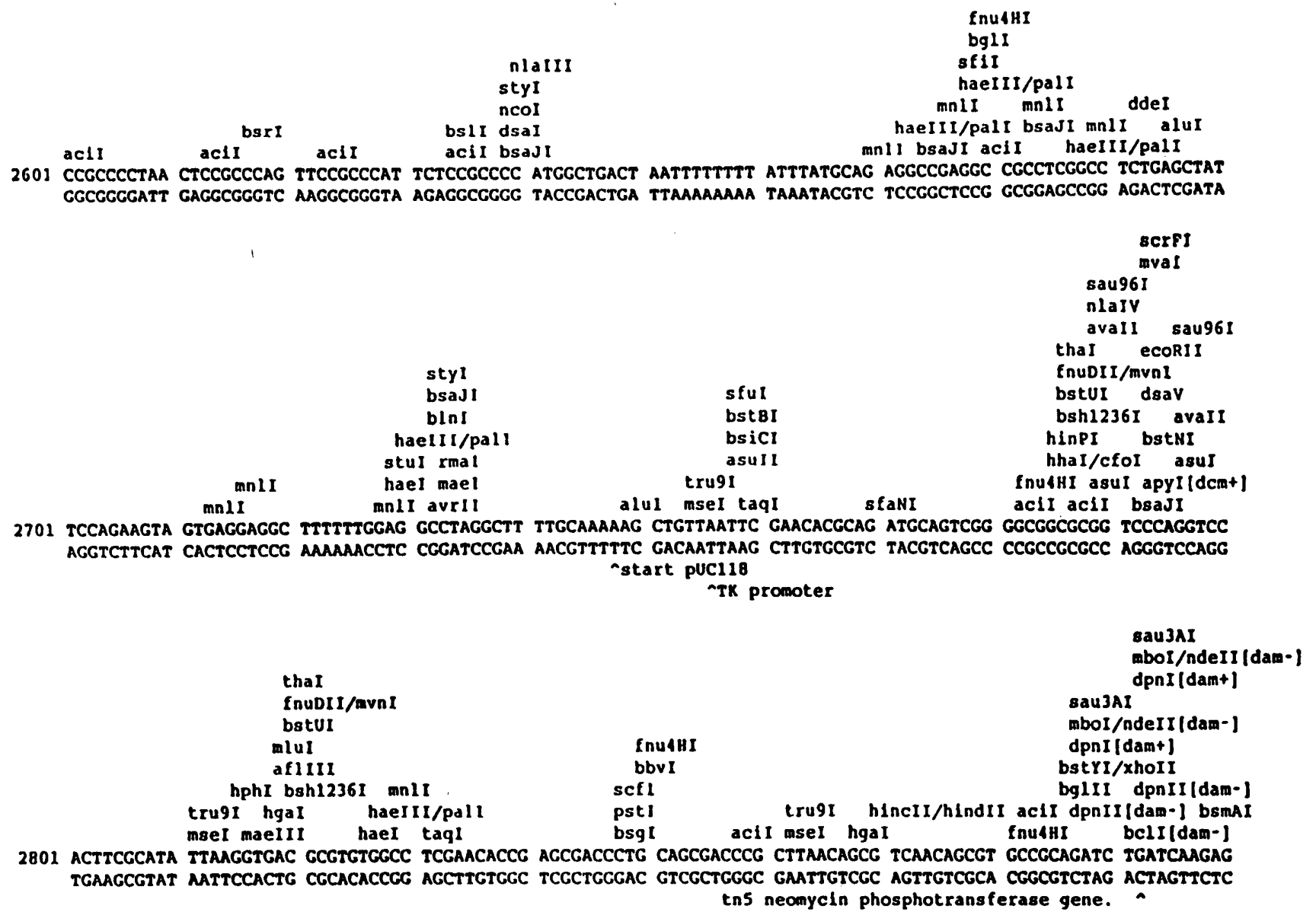

FIG. 6J

08/793653
PCT/US96/20718

FIG. 6K

08/793653
PCT/US96/20718

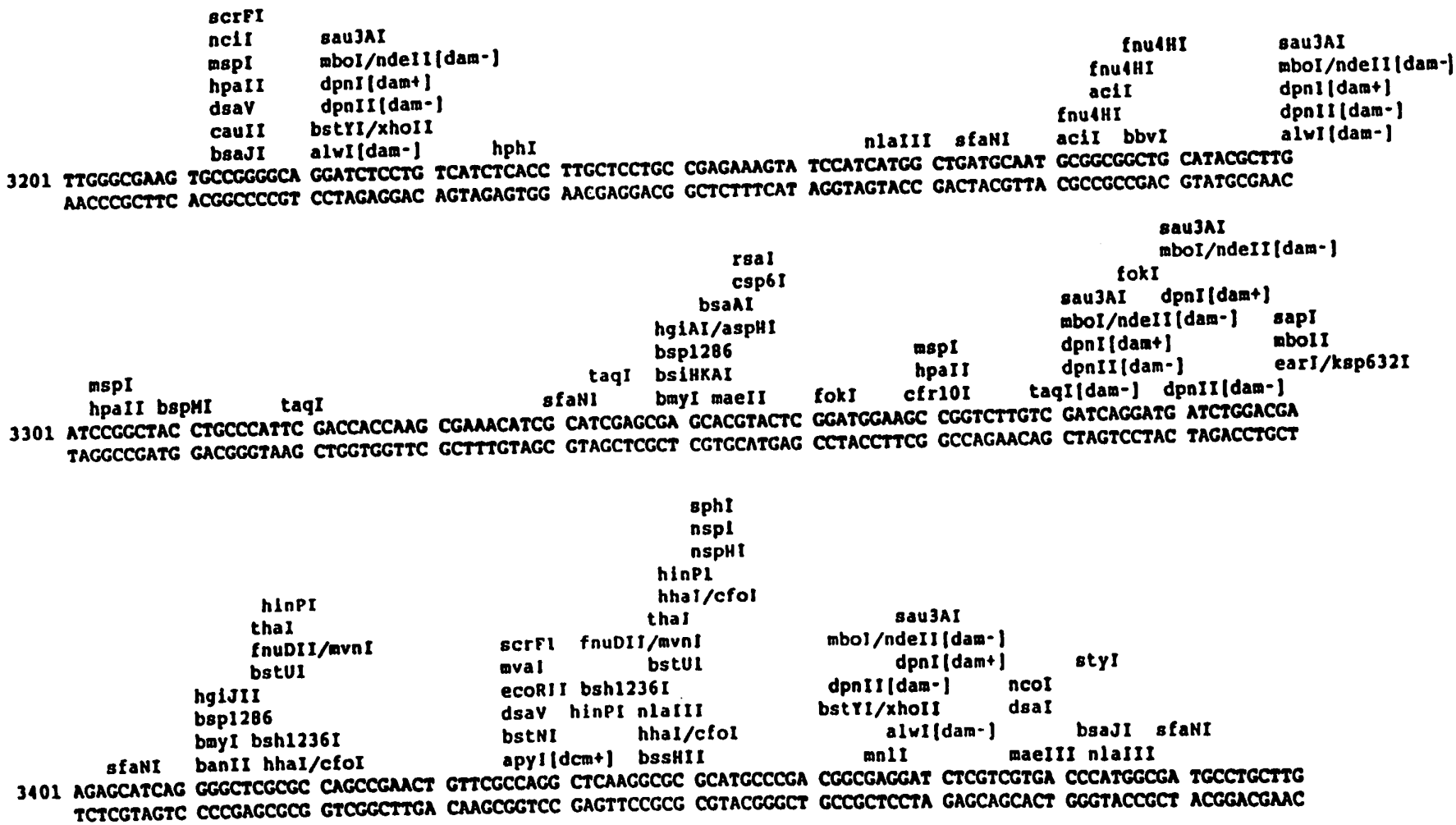

FIG. 6L

```
                                                            mspI               bslI
                                                            hpaII           sau96I
                              aciI                        naeI              avaII
                             fnu4HI                       cfr10I            asuI
                            haeIII/palI                  haeIII/palI       rsrII/cspI
                           eaeI           tfiI          eaeI               cpoI
             nlaIII        cfrI           hinfI  taqI   cfrI              aciI aciI
3501 CCGAATATCA TGGTGGAAAA TGGCCGCTTT TCTGGATTCA TCGACTGTGG CCGGCTGGGT GTGGCGGACC GCTATCAGGA CATAGCGTTG GCTACCCGTG
     GGCTTATAGT ACCACCTTTT ACCGGCGAAA AGACCTAAGT AGCTGACACC GGCCGACCCA CACCGCCTGG CGATAGTCCT GTATCGCAAC CGATGGGCAC

             sapI                                                                       hinPI
             mboII      fnu4HI                                         bsrBI            hhaI/cfoI
             earI/ksp632I                                              aciI    tfiI  fnu4HI
           eco57I aluI  aciI              acrI   mnlI                fnu4HI    hinfI bbvI sfaNI
3601 ATATTGCTGA AGAGCTTGGC GGCGAATGGG CTGACCGCTT CCTCGTGCTT TACGGTATCG CCGCTCCCGA TTCGCAGCGC ATCGCCTTCT ATCGCCTTCT
     TATAACGACT TCTCGAACCG CCGCTTACCC GACTGGCGAA GGAGCACGAA ATGCCATAGC GGCGAGGGCT AAGCGTCGCG TAGCGGAAGA TAGCGGAAGA

                                       taqI
                                      sfuI
                      aciI            bstBI                 hinlI/acyI                    tfiI       aciI
                  ddeI     pleI       bsiCI                 hgaI    bspHI                 hinfI     fnu4HI
             mboII  bsrBI  hinfI      asuII                 ahaII/bsaHI                 taqI      aciI
3701 TGACGAGTTC TTCTGAGCGG GACTCTGGGG TTCGAAATGA CCGACCAAGC GACGCCCAAC CTGCCATCAC GAGATTTCGA TTCCACCGCC GCCTTCTATG
     ACTGCTCAAG AAGACTCGCC CTGAGACCCC AAGCTTTACT GGCTGGTTCG CTGCGGGTTG GACGGTAGTG CTCTAAAGCT AAGGTGGCGG CGGAAGATAC
```

FIG. 6M

```
                                                                                                    scrFI
                                                                                                    nciI
                                                                                                    mspI
                                                                                                    hpaII
                                                                                                    dsaV
                                                                                                    cauII
                                                                                                    bslI
                                   hinlI/acyI                 thaI  sau3AI                         xmaI/pspAI
                                   hgaI                  bslI fnuDII/mvnI                          smaI
                                   ahaII/bsaiII        gsuI/bpmI   bstYI/xhoII                     scrFI
                               scrFI                  mnlI   hinPI alwI(dam-)                      nciI
                               nciI               sau3AI     hhaI/cfoI        gsuI/bpmI            dsaV
                               mspI     mspI      mboI/ndeII(dam-) mboI/ndeII(dam-)                cauII
                               hpaII    hpaII     dpnI(dam+) bstUI dpnI(dam+)                      bsaJI
                     tfiI      dsaV    naeI       dpnII(dam-) aciI dpnII(dam-)                    bsaJI
                     hinfI     cauII   cfr10I fokI alwI(dam-) bsh1236I    nlaIII      mboII  bslI avaI
3801 AAAGGTTGGG CTTCGGAATC GTTTTCCGGG ACGCCGGCTG GATGATCCTC CAGCGCGGGG ATCTCATGCT GGAGTTCTTC GCCCACCCCG GGAGATGGGG
     TTTCCAACCC GAAGCCTTAG CAAAAGGCCC TGCGGCCGAC CTACTAGGAG GTCGCGCCCC TAGAGTACGA CCTCAAGAAG CGGGTGGGGC CCTCTACCCC
                                                                           HSV1 tk terminator SmaI-PvuII  ^

                                                     hinPI
                                                     hhaI/cfoI
                                                    thaI
                                                    fnuDII/mvnI
                                      mspI          bstUI
                                      hpaII         bsh1236I
     mnlI                   bsmAI    bsaWI  nlaIV aciI
3901 GAGGCTAACT GAAACACGGA AGGAGACAAT ACCGGAAGGA ACCCGCGCTA TGACGGCAAT AAAAAGACAG AATAAAACGC ACGGGTGTTG GGTCGTTTGT
     CTCCGATTGA CTTTGTGCCT TCCTCTGTTA TGGCCTTCCT TGGGCGCGAT ACTGCCGTTA TTTTTCTGTC TTATTTTGCG TGCCCACAAC CCAGCAAACA

                            scrFI
                            mvaI
                            ecoRII
                            dsaV
                            bstNI
                            bsaJI
                           bslI
             aciI      sau96I                                                          thaI
            thaI       nlaIV                                                  haeIII/palI  fnuDII/mvnI
            fnuDII/mvnI    bsaJI                                     bslI     sau96I       bstUI
            bstUI      avaII                                     bsmAI       asuI          bsh1236I
            bsh1236I   asuI apyI(dcm+)        taqI              bsaI        nlaIV        aciI    mboII
4001 TCATAAACGC GGGGTTCGGT CCCAGGGCTG GCACTCTGTC GATACCCCAC CGAGACCCCA TTGGGGCCAA TACGCCCGCG TTTCTTCCTT TTCCCCACCC
     AGTATTTGCG CCCCAAGCCA GGGTCCCGAC CGTGAGACAG CTATGGGGTG GCTCTGGGGT AACCCCGGTT ATGCGGGCGC AAAGAAGGAA AAGGGGTGGG
```

FIG. 6N

```
                                  hgiJII                                           sau96I
                                  bsp1286                                          nlaIV
                                  bmyI                                             haeIII/palI
                               scrFI                                         sau96I
                               mvaI                                               nlaIV
                               ecoRII                                        hgiJII                     bslI
                               dsaV                                          eco0109I/draII          sau96I
                               bstNI                                              bsp1286                 nlaIV
                               bsaJI                                              bsp120I                 avaII styI
                               apyI(dcm+)                                         bmyI                    asuI  ncoI
                              bsaJI                                               banII                  ppuMI  dsaI
                            sau96I     bsl1                             xcmI asuI dsaI              nlaIV  bsaJI
           bslI             haeIII/palI  fnu4HI          fnu4HI               dsaI apaI bsaJI             eco0109I/draII
          bslI       hphI   asuI  banII  bbvI    maeII   aciI       aciI      bsaJI asuI             tth111I/aspI nlaIII
4101 CAACCCCCAA GTTCGGGTGA AGGCCCAGGG CTCGCAGCCA ACGTCGGGGC GGCAAGCCCG CCATAGCCAC GGGCCCCGTG GGTTAGGGAC GGGGTCCCCC
     GTTGGGGGTT CAAGCCCACT TCCGGGTCCC GAGCGTCGGT TGCAGCCCCG CCGTTCGGGC GGTATCGGTG CCCGGGGCAC CCAATCCCTG CCCCAGGGGG

                                                                                                   nlaIII
                                                                                                  styI
                                                                   sau96I                         ncoI            haeIII/palI
                                                                   avaII                          dsaI           haeI
                                                                   asuI     bsrI        ddeI      bsaJI       fokI
4201 ATGGGGAATG GTTTATGGTT CGTGGGGGTT ATTCTTTTGG GCGTTGCGTG GGGTCAGGTC CACGACTGGA CTGAGCAGAC AGACCCATGG TTTTTGGATG
     TACCCCTTAC CAAATACCAA GCACCCCCAA TAAGAAAACC CGCAACGCAC CCCAGTCCAG GTGCTGACCT GACTCGTCTG TCTGGGTACC AAAAACCTAC

                                                                                                     aciI
                                                                                                    thaI
                                                                                                    fnuDII/mvnI  hinPI
                                                                                                    bstUI        hhaI/cfoI
      scrFI                                   hinlI/acyI                                      bsh1236I    nlaIV
      mvaI      sau96I                              ahaII/bsaHI                                    hinPI        narI
      ecoRII               thaI          scrFI                                              thaI          kasI
      dsaV         rsaI    fnuDII/mvnI   nciI                                               fnuDII/mvnI   hinlI/acyI
      bstNI     avaII nlaIII     bstUI          mspI                                              bstUI        hgiCI
      bslI      asuI nspI       hinPI           hpaII                                             bsh1236I     haeII
      bsaJI nlaIII   nspHI  bsrI bsh1236I       dsaV hgaI      fnu4HI                            aciI         banI
      apyI(dcm+)   aciI  csp6I  hhaI/cfoI       cauII          bbvI                           bslI hhaI/cfoI   ahaII/bsaHI
4301 GCCTGGGCAT GGACCGCATG TACTGGCGCG ACACGAACAC CGGGCGTCTG TGGCTGCCAA ACACCCCCGA CCCCCAAAAA CCACCGCGCG GATTTCTGGC
     CGGACCCGTA CCTGGCGTAC ATGACCGCGC TGTGCTTGTG GCCCGCAGAC ACCGACGGTT TGTGGGGGCT GGGGGTTTTT GGTGGCGCGC CTAAAGACCG
```

FIG. 6O

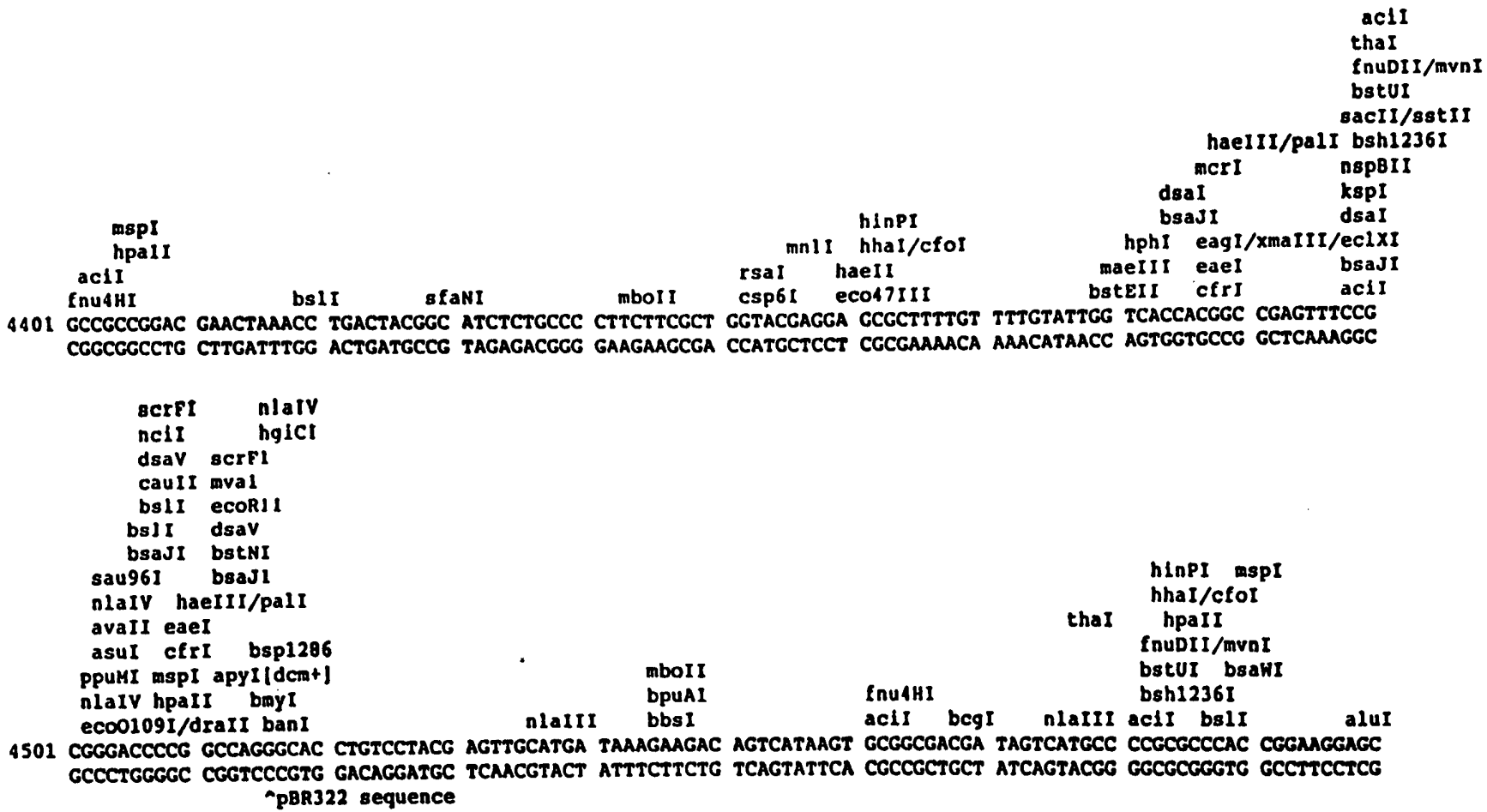

FIG. 6P

```
                                        fnu4HI
                                         haeIII/palI
                                          mcrI
                                          eagI/xmaIII/eclXI                          hinPI
                                          eaeI                                      thaI
                                         notI                                       fnuDII/mvnI
                                         fnu4HI                                     bstUI scfI     hinPI      hinPI
                                         aciI                                       bsh1236I       hhaI/cfoI  hhaI/cfoI
                                   mcrI  bsrBI aciI                             rsaI hhaI/cfoI   fnu4HI     tru9I aciI
      bsrI                     sfaNI    taqI cfrI   sfaNI                      csp6I    bslI     aciI       mseI bsh1236I
4601 TGACTGGGTT GAAGGCTCTC AAGGGCATCG GTCGAGCGGC CGCATCAAAG CAACCATAGT ACGCGCCCTG TAGCGGCGCA TTAAGCGCGG CGGGTGTGGT
     ACTGACCCAA CTTCCGAGAG TTCCCGTAGC CAGCTCGCCG GCGTAGTTTC GTTGGTATCA TGCGCGGGAC ATCGCCGCGT AATTCGCGCC GCCCACACCA
                                                  ^delta 3
                                                   ^M13 ori

              fnu4HI
            hinPI
            hhaI/cfoI                                  hinPI
           thaI                                        hhaI/cfoI
           fnuDII/mvnI                              rmaI                                                       mspI
           bstUI                                 hinPI  haeII                                                  hpaII
           bsh1236I     aciI                     hhaI/cfoI    bsrBI                                           naeI
      maeIII bbvI   maeIII                      haeII maeI    aciI            mboII                    maeII   cfr10I
4701 GGTTACGCGC AGCGTGACCG CTACACTTGC CAGCGCCCTA GCGCCCGCTC CTTTCGCTTT CTTCCCTTCC TTTCTCGCCA CGTTCGCCGG CTTTCCCCGT
     CCAATGCGCG TCGCACTGGC GATGTGAACG GTCGCGGGAT CGCGGGCGAG GAAAGCGAAA GAAGGGAAGG AAAGAGCGGT GCAAGCGGCC GAAAGGGGCA

                      nlaIV
                     hgiJII
                     bsp1286                                 nlaIV                                           maeII      haeIII/palI
                     bmyI                                    hgiCI   taqI                                    draIII     sau96I
      aluI           banII          nlaIV                    banI mnlI                             hphI      bsaAI      asuI
4801 CAAGCTCTAA ATCGGGGGCT CCCTTTAGGG TTCCGATTTA GTGCTTTACG GCACCTCGAC CCCAAAAAAC TTGATTTGGG TGATGGTTCA CGTAGTGGGC
     GTTCGAGATT TAGCCCCCGA GGGAAATCCC AAGGCTAAAT CACGAAATGC CGTGGAGCTG GGGTTTTTTG AACTAAACCC ACTACCAAGT GCATCACCCG

                                       maeII pleI              tru9I     pleI                                 bslI
                                      drdI   hinfI   maeII     mseI      hinfI         bsrI                  bslI   avaI
4901 CATCGCCCTG ATAGACGGTT TTTCGCCCTT TGACGTTGGA GTCCACGTTC TTTAATAGTG GACTCTTGTT CCAAACTGGA ACAACACTCA ACCCTATCTC
     GTAGCGGGAC TATCTGCCAA AAAGCGGGAA ACTGCAACCT CAGGTGCAAG AAATTATCAC CTGAGAACAA GGTTTGACCT TGTTGTGAGT TGGGATAGAG
```

FIG. 6Q

FIG. 6R

```
                                                                               scrFI
                                                                               nciI
                                                         aciI                  mspI
                                                         thaI                  hpaII
                                                         fnuDII/mvnI           dsaV
                                                         bstUI                 cauII
   maeII             hgiAI/aspHI                         bsh1236I            hinII/acyI
   psp1406I          bsp1286  tru9I                      hinPI               hgaI                                    aciI
   xmnI              bsiHKAI  mseI                       hhaI/cfoI           ahaII/bsaHI    bcgI    mcrI  fnu4HI
   asp700            bmyI    ahaIII/draI
5501 GAACGTTTTC CAATGATGAG CACTTTTAAA GTTCTGCTAT GTGGCGCGGT ATTATCCCGT GATGACGCCG GGCAAGAGCA ACTCGGTCGC CGCATACACT
     CTTGCAAAAG GTTACTACTC GTGAAAATTT CAAGACGATA CACCGCGCCA TAATAGGGCA CTACTGCGGC CCGTTCTCGT TGAGCCAGCG GCGTATGTGA

                                rsaI
                                csp6I  bsrI                                                            fnu4HI
       ddeI                     scaI hphI   maeIII     sfaNI     fokI  nlaIII                          bbvI          nlaIII
5601 ATTCTCAGAA TGACTTGGTT GAGTACTCAC CAGTCACAGA AAAGCATCTT ACGGATGGCA TGACAGTAAG AGAATTATGC AGTGCTGCCA TAACCATGAG
     TAAGAGTCTT ACTGAACCAA CTCATGAGTG GTCAGTGTCT TTTCGTAGAA TGCCTACCGT ACTGTCATTC TCTTAATACG TCACGACGGT ATTGGTACTC

                                                sau96I
                                                avaII
                                         sau3AI asuI                                                  nlaIII
                haeIII/palI              mboI/ndeII(dam-)                                        sau3AI maeIII
                eaeI                     dpnI(dam+)                                              mboI/ndeII(dam-)      sau3AI
                cfrI                     dpnII(dam-)                                             dpnI(dam+)            mboI/ndeII(dam-)
                fnu4HI                   pvuI/bspCI                                              alwI(dam-)            dpnI(dam+)
                aciI                     mcrI  mnlI           aluI  aciI                   nlaIII dpnII(dam-)          dpnII(dam-)
5701 TGATAACACT GCGGCCAACT TACTTCTGAC AACGATCGGA GGACCGAAGG AGCTAACCGC TTTTTTGCAC AACATGGGGG ATCATGTAAC TCGCCTTGAT
     ACTATTGTGA CGCCGGTTGA ATGAAGACTG TTGCTAGCCT CCTGGCTTCC TCGATTGGCG AAAAAACGTG TTGTACCCCC TAGTACATTG AGCGGAACTA

                                                                                                hinPI
              mspI                                                                            mstI
              hpaII                                                                           avlII/fspI       bsrI
             bsaWI                                                            fnu4HI        maeII hhaI/cfoI   tru9I
        nlaIV     aluI                                  maeIII     sfaNI      bbvI         psp1406I           mseI
5801 CGTTGGGAAC CGGAGCTGAA TGAAGCCATA CCAAACGACG AGCGTGACAC CACGATGCCA GCAGCAATGG CAACAACGTT GCGCAAACTA TTAACTGGCG
     GCAACCCTTG GCCTCGACTT ACTTCGGTAT GGTTTGCTGC TCGCACTGTG GTGCTACGGT CGTCGTTACC GTTGTTGCAA CGCGTTTGAT AATTGACCGC
```

FIG. 6S

FIG. 6T

```
                                       sau3AI
                                       mboI/ndeII[dam-]
                                       dpnI[dam+]   sau3AI          thaI
                                       dpnII[dam-]  mboI/ndeII[dam-]
                                       bstYI/xhoII  dpnI[dam+]      fnuDII/mvnI
                              sau3AI   alwI[dam-]   dpnII[dam-]     bstUI
                              mboI/ndeII[dam-]      alwI[dam-]      bsh1236I
                              dpnI[dam+] mboII[dam-]               hinPI      fnu4HI
           ddeI hgaI          dpnII[dam-]           bstYI/xhoII    hhaI/cfoI  bbvI
6301 TTCGTTCCAC TGAGCGTCAG ACCCCGTAGA AAAGATCAAA GGATCTTCTT GAGATCCTTT TTTTCTGCGC GTAATCTGCT GCTTGCAAAC AAAAAAACCA
     AAGCAAGGTG ACTCGCAGTC TGGGGCATCT TTTCTAGTTT CCTAGAAGAA CTCTAGGAAA AAAAGACGCG CATTAGACGA CGAACGTTTG TTTTTTTGGT

                          sau3AI
                          mboI/ndeII[dam-]
                          dpnI[dam+]
                          dpnII[dam-]
                         alwI[dam-]
           aciI          mspI                                 bsrI          hinPI                rmaI
     aciI  nspBII        hpaII     aluI                    maeIII  eco57I   hhaI/cfoI            maeI
6401 CCGCTACCAG CGGTGGTTTG TTTGCCGGAT CAAGAGCTAC CAACTCTTTT TCCGAAGGTA ACTGGCTTCA GCAGAGCGCA GATACCAAAT ACTGTCCTTC
     GGCGATGGTC GCCACCAAAC AAACGGCCTA GTTCTCGATG GTTGAGAAAA AGGCTTCCAT TGACCGAAGT CGTCTCGCGT CTATGGTTTA TGACAGGAAG

                                                                                     fnu4HI
                                                                          alwNI    bbvI
                haeIII/palI                                               bsrI  fnu4HI
          bslI     haeI               scfI     aciI      mnlI          maeIII   bbvI     bsrI
6501 TAGTGTAGCC GTAGTTAGGC CACCACTTCA AGAACTCTGT AGCACCGCCT ACATACCTCG CTCTGCTAAT CCTGTTACCA GTGGCTGCTG CCAGTGGCGA
     ATCACATCGG CATCAATCCG GTGGTGAAGT TCTTGAGACA TCGTGGCGGA TGTATGGAGC GAGACGATTA GGACAATGGT CACCGACGAC GGTCACCGCT

             scrFI                                        mcrI                hgiAI/aspHI
             nciI                                      nspBII                 bsp1286
             mspI                          mspI        fnu4HI                 bsiHKAI
             hpaII                         hpaII       bbvI                   bmyI
             dsaV    pleI                 bsaWI     hinPI aciI                apaLI/snoI
             cauII   hinfI             maeIII       hhaI/cfoI                 alw44I/snoI   aluI
6601 TAAGTCCTGT CTTACCGGGT TGGACTCAAG ACGATAGTTA CCGGATAAGG CGCAGCGGTC GGGCTGAACG GGGGGTTCGT GCACACAGCC CAGCTTGGAG
     ATTCAGCACA GAATGGCCCA ACCTGAGTTC TGCTATCAAT GGCCTATTCC GCGTCGCCAG CCCGACTTGC CCCCCAAGCA CGTGTGTCGG GTCGAACCTC
```

FIG. 6U

```
                                                                                                   mspI
                                                          hinPI                                    hpaII
                                                          hhaI/cfoI                                bslI     fnu4HI
                        ddeI      scfI                   haeII                          aciI      bsaWI    aciI
6701 CGAACGACCT ACACCGAACT GAGATACCTA CAGCGTGAGC ATTGAGAAAG CGCCACGCTT CCCGAAGGGA GAAAGGCGGA CAGGTATCCG GTAAGCGGCA
     GCTTGCTGGA TGTGGCTTGA CTCTATGGAT GTCGCACTCG TAACTCTTTC GCGGTGCGAA GGGCTTCCCT CTTTCCGCCT GTCCATAGGC CATTCGCCGT

                                      scrFI
                                      mvaI          scrFI
                                      ecoRII  mvaI
                                      dsaV    ecoRII
                                      bstNI         dsaV
                       hinPI  mnlI    bsaJI         bstNI                                                taqI
                       hhaI/cfoI  aluI apyI[dcm+]  apyI[dcm+]                           mnlI  drdI   hgaI
6801 GGGTCGGAAC AGGAGAGCGC ACGAGGGAGC TTCCAGGGGG AAACGCCTGG TATCTTTATA GTCCTGTCGG GTTTCGCCAC CTCTGACTTG AGCGTCGATT
     CCCAGCCTTG TCCTCTCGCG TGCTCCCTCG AAGGTCCCCC TTTGCGGACC ATAGAAATAT CAGGACAGCC CAAAGCGGTG GAGACTGAAC TCGCAGCTAA

                                                  aluI                                                 tru9I
                               nlaIV             pvuII                                      hinPI      mseI
          sfaNI              aciI                nspBII                bsrI       aciI      hhaI/cfoI  aseI/asnI/vspI
6901 TTTGTGATGC TCGTCAGGGG GGCGGAGCCT ATGGAAAAAC GCCAGCTGGC ACGACAGGTT TCCCGACTGG AAAGCGGGCA GTGAGCGCAA CGCAATTAAT
     AAACACTACG AGCAGTCCCC CCGCCTCGGA TACCTTTTTG CGGTCGACCG TGCTGTCCAA AGGGCTGACC TTTCGCCCGT CACTCGCGTT GCGTTAATTA
                                                   ^delta1.PVU

                                 scrFI
                                 mvaI
                                 ecoRII
                                 dsaV
                            nlaIV bstNI
                mnlI        hgiCI apyI[dcm+]                mspI                          aciI
            maeIII          banI bsaJI                      hpaII                       bsrBI
7001 GTGAGTTACC TCACTCATTA GGCACCCCAG GCTTTACACT TTATGCTTCC GGCTCGTATG TTGTGTGGAA TTGTGAGCGG ATAACAATTT CACACAGGAA
     CACTCAATGG AGTGAGTAAT CCGTGGGGTC CGAAATGTGA AATACGAAGG CCGAGCATAC AACACACCTT AACACTCGCC TATTGTTAAA GTGTGTCCTT

                              tru9I
                              mseI
                             aseI/asnI/vspI
                            xmnI
        aluI      nlaIII    asp700
7101 ACAGCTATGA CCATGATTAC GAATTAA
     TGTCGATACT GGTACTAATG CTTAATT
```

>length: 7127

aatII(GACGTC): 150 203 286 472 5182

FIG. 6V